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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/543,188	04/05/2000	David J. Hammond	18242-507 (VI-7)	6857

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EXAMINER

LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 08/14/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/543,188

Applicant(s)

HAMMOND ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-75 is/are pending in the application.
- 4a) Of the above claim(s) 3-6, 30-38, and 40-75 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5, 7-15, 17-29 and 39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 and 12.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I(C) in Paper No. 15 is acknowledged.
2. It is here noted that the applicants have misinterpreted the restriction among the sequences within Group I(C) as a species election. The restriction between sequences required an election of inventions, not species. Each sequence is a distinct invention as each sequence has a different structure, and because the functions of polypeptides are sequence driven, each peptide also has a different function.
3. Claims 3, 4, 6, 30-38, 40-75 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 15.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
5. Claim 9 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility. This rejection is based on an assumption that the claim is intended to read on a peptide comprising SEQ ID NO: 34, the retro-inverso isomer of SEQ ID NO: 1. In such a case, the applicant has not provided a utility for the claim, because although the applicant does discuss retro-inverso isomers in the specification, the applicant has not stated or described any naturally occurring, or other, proteins or polypeptides that comprise the sequence of SEQ ID NO: 34.

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Claim 10 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, 5, 7-15 and 18-29 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some specific peptide ligands, does not reasonably provide enablement for any ligand, or any peptide ligand, to the prion protein, or to the fragment of the protein represented by SEQ ID NO: 1. Further, the applicant is also not enabled for all of the peptide ligands of claim 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

A claim is commensurate in scope with the enablement when the applicant has provided sufficient disclosure to enable one skilled in the art to practice the claimed invention without undue experimentation. In re Wands, 8 USPQ2d 1400, 1404 (CAFC 1988). There must be a “reasonable correlation” between the scope of enablement and the scope of the claims. In re Fisher, 166 U.S.P.Q. 18, 24 (CCPA 1970). In the present case, this correlation requires that “there must be sufficient disclosure, either through illustrative examples or terminology, to teach

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those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." See, In re Vaeck, 20 U.S.P.Q.2d 1438, 1444 (CAFC 1991) (explaining why disclosure of one working examples in an unpredictable art was insufficient to enable claims to a generic claim covering bacteria from many different genera). Therefore, although neither working examples, nor an explanation of how the invention work are required, they are factors that may be considered when determining the scope of enablement provided by the applicant.

The applicant has disclosed methods of screening for ligands. However, the applicant has provided little guidance, in comparison to the number of potential ligands, to lead one skilled in the art to molecules likely to bind prions. The applicant discloses that the ligands of the invention may be "nucleic acids, peptides, polypeptides, peptidomimetics, carbohydrates, lipids, or other organic (carbon containing) or inorganic molecules." Specification, pp. 3-4. The applicant has therefore stated that the ligand may be any type of molecule at all, so long as it is under 6 kDa. The specification also states the it is "not possible to conclude from a single experiment the affinity of octapeptide for ligand since the stoichiometry of binding is not known..." Thus, the applicant has also stated that, with regards to a specific fragment of the prion protein, one skilled in the art cannot easily tell which peptides are likely to be found to be ligands. This statement lends support for a lack of enablement rejection of claims to all prion ligands (claim 1), all prion peptide ligands (claim 7), and all peptide ligands according to the formula of claim 15.

The statement is an admission that the applicant is not enabled for any peptide ligand. This is because one skilled in the art cannot tell which peptides are likely to have an affinity to a

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specific region of the prion protein, and because the applicant has provided only a limited number of examples and a limited amount of guidance to lead to such peptides. As the number of examples provided is not sufficient guidance to lead one in the art to every peptide ligand to prions, the applicant cannot be enabled for every peptide that can bind a prion protein. This is demonstrated by the fact that other peptides than those disclosed by the applicants have been shown to bind prions (see, references cited in art rejections below), and one in the art would not have been lead to such other peptides by the applicant's disclosure.

Further, the applicant is not enabled for the peptides of claim 15 because the applicant has not shown that all of the peptides included by the claimed formula will work, or are likely to work. The applicant has disclosed as operable only 6 of the peptides included by the formula of claim 15. The applicant has also disclosed numerous peptides not according to that formula that bind to prions. See, Table 1, Application, p. 5. Thus, the applicants have not shown any particular affinity that sequences of the disclosed formula may have towards prions. In fact, as the disclosure describes only 6 within the formula, and a great number without, the disclosure as a whole indicates that random peptides not necessarily sharing any particular sequence homology bind to prions. The fact that the six disclosed sequences were shown to work does not prove that the generic formula has any relation to the binding capacity as the six peptides formed the basis from which the formula was derived. App., p. 32 (showing how the consensus sequence for the formula was derived). One could just have easily taken any other six of the peptides of table 1, and derived a different consensus formula.

By indicating that only the original 6 of a potential 360 peptides ($3 \times 3 \times 5 \times 2 \times 1 \times 4$) are operable, and showing a large number of peptides not within the formula that bind to prions, the

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applicant has failed to provide sufficient evidence that the undisclosed peptide from the 360 within the formula are likely to bind prions. Nor has the applicant provided any guidance as to which of those undisclosed peptides are more likely than not to act as ligands. Thus, one skilled in the art who desired to practice the invention would be left to determine on their own which, if any, of the undisclosed peptides would act as ligands. Therefore, while the number of potential peptides is not excessively large, and despite the ease of running an assay to determine the binding ability of the peptides; the combination of the lack of guidance and the admitted unpredictability involved in identifying ligands lead to the conclusion that the practice of the invention to the full scope of the claims would require undue experimentation.

Since the applicants have indicated that one skilled in the art cannot tell which molecules of a single type of molecule (the peptides) may be used as ligands, they cannot have enabled those in the art for any ligand molecule at all, as they have provided no guidance outside of the identification of relatively small number of peptides. The applicants have not provided a disclosure that would enable one skilled in the art to make or use any prion ligand without undue experimentation.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim reads:

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The peptide ligand of claim 7, wherein said peptide ligand comprises the amino acid sequence of a peptide with the amino acid sequence of SEQ ID NOs: 3-29 or SEQ ID NO: 30.

It is unclear if the applicant intends to either a peptide containing all of the sequences of SEQ ID NOs: 3-29 or a peptide containing SEQ ID NO: 30; or if the applicant intended to claim a peptide comprising one of the sequences of SEQ ID Nos: 3-30.

10. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim reads on a ligand to a polypeptide comprising the retro-inverso isomer of SEQ ID NO: 34. Such a polypeptide would read on a polypeptide that comprises the sequence of SEQ ID NO: 1, as that sequence is the retro-inverso isomer of SEQ ID NO: 34. It is therefore unclear whether the applicant intended to claim a ligand to a polypeptide comprising SEQ ID NO: 1, in which case the claim is objected to for failure to be further limiting, or if the applicant intended to claim a ligand that binds a polypeptide comprising SEQ ID NO: 34.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

12. Claims 1, 2, 5, 7, 8, 10, 18, 20, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by WO document 96/39834, naming Soto-Jara et al. as inventors (Soto-Jara). The claims read on peptides of less than 20 amino acid residues that bind to proteins comprising of either SEQ ID NO: 1 or retro-inverso isomers thereof, and to compositions comprising the peptides.

Soto-Jara teaches two peptides of respectively 12 and 7 amino acids that bind to a prion protein. Pp. 16-17. The peptides are disclosed as being able to bind to a prion protein that has the sequence Gly-Ala- Ala-Ala Ala-Gly- Ala-Val-Val-Gly-Gly-Leu at residues 114-125. P. 16, lines 16-19. The human prion protein disclosed in U.S. Patent Number 6,211,149 as SEQ ID NO: 20 has those residues in its sequence at positions 114-125, and also has SEQ ID NO: 1 of the present application as residues 64-71. Because the peptides disclosed by Soto-Jara are able to bind a protein comprising SEQ ID NO: 1, and because those peptides are less than 20 amino acids long, Soto-Jara anticipates the claims to the peptides. The reference also teaches compositions comprising the peptides. P. 19. As the applicant has not stated how a ligand isolated by the method referenced in claim 39 structurally affects the ligand, the claim is being interpreted to read on any prion ligand.

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13. Claims 1,2, 5, 7, 8, 10, 18, 20, and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 6,211,149, issued to Chesebro et al. (Chesebro). The claims read on peptides of less than 20 amino acid residues that bind to proteins comprising of either SEQ ID NO: 1 or retro-inverso isomers thereof, and to compositions comprising the peptides.

Chesebro describes polypeptides, including some with less than 20 amino acids (see e.g. SEQ ID NOs: 1-4 of the patent) that bind to prion proteins to prevent them from forming their protease resistant forms. Col. 3, lines 13-51. Among the prion proteins which can be bound by the polypeptides are human, mouse, and hamster proteins. Col. 6, lines 54-62. Each of these proteins comprises the sequence Gly-Trp-Gly-Gln-Phe-His-Gly-Gly (SEQ ID NO: 1 of the present application). See, patent sequence listing, SEQ ID NO: 18 (res. 34-41), SEQ ID NO: 19 (res. 63-70), and SEQ ID NO: 20 (res. 56-64). Because the patent discloses peptides less than 20 amino acids that bind to proteins comprising SEQ ID NO: 1, the patent anticipates the stated claims. As Chesebro also discloses pharmaceutical compositions comprising the peptides (col. 4, lines 10-12), claim 20 is also anticipated.

14. Claims 1, 2, 5, 7, 8, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,750,361, issued to Stanley B. Pruisner. The claims are described above. The reference teaches a number of peptides (SEQ ID NOs: 3,4,5, and 6) that are disclosed as being capable of binding to prion proteins. Col. 6-7, and col. 7, lines 60-65. The sequences disclosed as SEQ ID NOs: 3 and 4 are only 14 amino acids in length, thereby anticipating claim 18. Because the reference discloses peptides of less than 20 amino acids that bind to prions, which contain SEQ ID NO: 1, and some of which contain SEQ ID NO: 2, the identified claims are anticipated.

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Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. Claims 11, and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chesebro, in view of U.S. Patent Number 6,221,614, issued to Prusiner et al. (the 614 patent). Claim 11 describes a peptide ligand that binds the polypeptide containing SEQ ID NO: 1 in the presence of a metal. Claims 20-24 describe a composition comprising either one of the peptide ligands. The later claims also describe a composition wherein the composition comprises a solid support, and wherein the solid support is either a resin or a membrane. The teachings of Chesebro are described above.

The 614 patent teaches a method of removing prion peptides from blood by attaching one or more complexing agents (ligands) to a solid support. Col 9, lines 36-39; and col. 10, lines 32-35, and 58-60. The ligands may comprise metallic salts of the ligands (col. 9, lines 14-17) or be bound to a high density metal (col. 11, lines 17-20), therefore the reference teaches that the ligands are able to bind prions in the presence of a metal. The solid supports may comprise membranes (col. 9, lines 14-17), or to other matrices, such as agarose and polymethacrylate. Col. 12, lines 40-54. Agarose is one of the resins disclosed by Patent number 5,541,294, a patent references in the specification (p. 10) as disclosing resins suitable for removing agents from blood. Polyemthacrylate is disclosed as a resin on page 17 of the specification in the present

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application. Although the 614 patent teaches the use of peptides, it does not teach the use of peptides with 20 or fewer amino acid residues.

From the combination of the references, it would have been obvious to one of ordinary skill in the art to use the peptides taught by Chesebro in the method taught by the 614 patent. This is because the 614 patent teaches the use of peptides that can bind prions, and Chesebro teaches such peptides. One of ordinary skill in the art would have had a reasonable expectation that the peptides taught by Chesebro would be operative in the methods taught by the 614 patent.

Allowable Subject Matter

17. Claim 16 is allowed insofar as it reads on a peptide ligand comprising the sequence of SEQ ID NO: 23. Peptide ligands to prion polypeptides comprising the sequence of SEQ ID NO: 23 appear to be free of prior art, and otherwise allowable.

Conclusion

18. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

Hornshaw et al., Bio-chemical and Biophysical Research Communications, 214(3):993-999 (1995). This article teaches that the region of the prion protein to which the peptides of the current application bind, also binds to copper ions in vivo. The article further teaches that copper binding to this region may be a part of the cause for the conformational change of the prion protein folding that leads to the protein's pathogenic state. However, Stöckel et al., Biochemistry 37(20): 8175-7193 (1998) states that it is unknown whether copper binding of the proteinase-resistant prion protein is involved in neurodegenerative prion disease. Stöckel, p.7191. Neither article teaches peptides or other ligands that may bind to the protein at the copper-binding site.

WO document 00/02575, naming Hammond et al as inventors. This published PCT application claims a kit for detecting prion proteins which comprises an agent capable of

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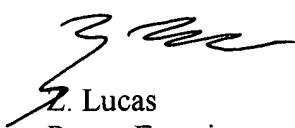
binding to the GLN-PRO-HIS residues of a prion protein. As this sequence is part of SEQ ID NO: 1 of the present application, a sequence required to be in the peptide to which the claimed ligand binds, the reference is deemed relevant. However, the reference does not disclose a ligand of less than 6 kDa or a peptide of 20 amino residues or less. The publication is therefore not applicable to the claims at hand.

Brimacombe et al., Biochem. J., 342: 605-613 1999). This article teaches that heparin can bind to prion proteins in the presence of copper. The article is relevant in that most prions contain the sequence represented by SEQ ID NO: 1 (see, Chesebro, above), and that that sequence is the binding site for copper (see, Hornshaw above) indicating that the prions of Brimacombe also contain that sequence. However, the reference is not being cited as prior art both because the molecular weight of the polyanions are not disclosed, and because the reference does not disclose the concentration of the copper.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Z. Lucas
Patent Examiner
August 9, 2002


JAMES HOUSEL
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